WEST Search History

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DATE: Friday, November 17, 2006

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
☐	L26	L16 and (x)adj(chromosome)	35
☐	L25	L24 and anti-VEGF-D	22
☐	L24	L22 and (homology)adj(domain)	43
☐	L23	L22 and (full)adj(lengh)	0
☐	L22	(VEGF-D)same(antibod?)	106
☐	L21	L17 and VEGF-D	28
☐	L20	L18 and (VEGF)adj(antibod?)	14
☐	L19	L18 and anti-VEGF?	0
☐	L18	L17 and (detection)	313
☐	L17	L16 and (brain)adj(tissue)	398
☐	L16	(glioblastoma)adj(multiforme)	1489
	DB=USPT; PLUR=YES; OP=OR		
☐	L15	L14 and VEGF-D	5
☐	L14	(530/388.23).ccls.	376
☐	L13	L12 and VEGF-D	4
☐	L12	(435/7.23).ccls.	1280
☐	L11	L10 and VEGF-D	26
☐	L10	(435/7.1).ccls.	6457
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
☐	L9	L7 and VEGF-D	7
☐	L8	(gibo)adj(denise)	9
☐	L7	(debinski)adj(waldemar)	34
☐	L6	(debinski)adj(waldmar)	0
☐	L5	L1 and (homology)adj(domain)	43
☐	L4	L3 and (brain)adj(tissue)	22
☐	L3	L2 and detection	92
☐	L2	L1 and cancer	110
☐	L1	(VEGF)adj(D)same(antibod?)	116

END OF SEARCH HISTORY

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FILE 'HOME' ENTERED AT 12:52:17 ON 17 NOV 2006

=> file meline embase biosis scisearch caplus
'MELINE' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available.  If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
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MULTIFILE PROCESSING IS NOT ALLOWED IN FILE 'HOME'
The file entered is not valid in multifile processing.  Enter "HELP
DUFILES" to see a list of the valid files.
ENTER A FILE NAME OR (IGNORE):embase
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.42       0.42

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     5.22       5.64

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=> s VEGFR
L1         9340 VEGFR

=> s l1 and KDR
L2         1922 L1 AND KDR

=> s l2 and glioblastoma mutliforme
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L3            0 L2 AND GLIOBLASTOMA MUTLIFORME

=> s detection
L4      2189885 DETECTION

=> s l4 and VEGF
L5         1812 L4 AND VEGF

=> s l5 and glioblastoma multiforme
L6           10 L5 AND GLIOBLASTOMA MULTIFORME

=> dup remove l6
PROCESSING COMPLETED FOR L6
L7             6 DUP REMOVE L6 (4 DUPLICATES REMOVED)

=> d l7 1-6 cbib abs

L7   ANSWER 1 OF 6     MEDLINE on STN                    DUPLICATE 1
2006476973.    PubMed ID: 16900782.   Up-regulation of VEGF
     expression and related neo-angiogenesis in childhood high-grade gliomas:
     implications for anti-angiogenic anti-neoplastic therapy. Bodey Bela;
     Siegel Stuart E; Kaiser Hans E. (Department of Pathology, University of
     Southern California, Keck School of Medicine, Los Angeles, USA..
     Bodey18@aol.com) . In vivo (Athens, Greece), (2006 Jul-Aug) Vol. 20, No.
     4, pp. 511-8.  Journal code: 8806809. ISSN: 0258-851X. Pub. country:
     Greece. Language: English.
AB   Vascular endothelial growth factor (VEGF) is a homodimeric,
     disulfide-linked glycoprotein which exhibits endothelial cell-specific
     mitogenic properties.  VEGF is also a potent inducer of vascular
     permeability.  There is considerable experimental evidence that
     VEGF isoforms are strongly involved in provoking neoangiogenesis
     of neoplastic cells and, consequently, the growth and progression of
     primary neoplasms (i.e., astrocytic gliomas), including the formation of
     an invasive and metastatic immunophenotype (IP).  During this
     immunohistochemical study, the presence and tissue localization of VEGF121
     was observed in anaplastic, high-grade astrocytomas (AAs) and in
     glioblastoma multiforme (GBMs) employing the specific
     monoclonal antibody against it.  A sensitive, four-step, alkaline
     phosphatase-conjugated antigen detection technique was used.
     The immunoreactivity demonstrated a cytoplasmic, cell surface and
     extracellular matrix localization pattern in more than 90% of the tumor
     cells, with high intensity immunoreactivity (++++, A,B) in every
     high-grade astrocytic glioma tissue.  VEGF121 expression was identified
     mostly within the cytoplasm of tumor cells, suggesting an embryonic,
     undifferentiated and more malignant cellular IP of high-grade gliomas.
     Tumor-related neo-angiogenesis and endothelial cell proliferation were
     also present.  The great majority of high-grade astrocytic gliomas are
     incurable with the three classic therapeutic modalities.  In the future,
     the development of targeted anti-neoplastic treatment strategies, adapted
     to individual patients, will require molecular identification of the
     different classes of neoplasm (including subtypes of astrocytomas)
     according to their stages, biology, prognosis and therapeutic options.

L7   ANSWER 2 OF 6  CAPLUS  COPYRIGHT 2006 ACS on STN
2005:1242850   Document No. 143:476225  Over-expression of tumor antigen Fra-1
     in glioblastoma multiforme and inhibition of Fra-1
     binding to a VEGF-D promoter for treating brain cancer.
     Debinski, Waldemar; Gibo, Denise M. (The Penn State Research Foundation,
     USA).  U.S. Pat. Appl. Publ. US 2005260649 A1 20051124, 42 pp.,
     Cont.-in-part of U.S. 6,884,581.  (English).  CODEN: USXXCO.  APPLICATION:
     US 2005-104137 20050412.  PRIORITY: US 2001-268089P 20010212; US
     2002-75499 20020212.
AB   The invention relates to the discovery that glioblastoma
     multiforme (GBM) strongly expresses Fra-1, an AP-1 transcription
     factor.  The gene for VEGF-D, a vascular endothelial growth
```

factor that plays a role in angiogenesis, harbors an optimal AP-1 binding site within its promoter region. When heterodimerized with c-Jun, Fra-1 binds to the AP-1 site within the VEGF-D gene promoter and activates expression of VEGF-D. Based on this discovery, central nervous system (CNS) cancers such as GBM can be diagnosed and treated using Fra-1 as a target tumor antigen. In addition, by disrupting the interaction between Fra-1 and the VEGF-D gene promoter, tumor angiogenesis can be inhibited. Cancer in a brain tissue sample is detected by analyzing expression of Fra-1 in the sample. Brain cancer is treated by modulating Fra-1 gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with Fra-1 binding to a VEGF-D promoter.

L7 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2005:544537 Document No.: PREV200510328584. Quantum dot nanotechnology for detection of gene product upregulation in cultured glioblastoma multiforme (GBM) cells in response to hypoxia and radiation. Nowlan, A. W. [Reprint Author]; Nie, S.; Datta, M.; Kirubro, K.; Johnstone, P. A.; Brat, D. J.. Emory Univ, Winship Canc Inst, Atlanta, GA 30322 USA. International Journal of Radiation Oncology Biology Physics, (2005) Vol. 63, No. 2, Suppl. 1, pp. S476-S477.
Meeting Info.: 47th Annual Meeting of the American-Society-for-Therapeutic-Radiology-and-Oncology. Denver, CO, USA. October 16 -20, 2005. Amer Soc Therapeut Radiol & Oncol.
CODEN: IOBPD3. ISSN: 0360-3016. Language: English.

L7 ANSWER 4 OF 6 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
2003:289300 The Genuine Article (R) Number: 660UY. Analysis of the TP53 gene in laser-microdissected glioblastoma vasculature. Kulla A; Burkhardt K; Meyer-Puttlitz B; Teesalu T; Asser T; Wiestler O D; Becker A J (Reprint). Univ Bonn, Med Ctr, Dept Neuropathol, Sigmund Freud Str 25, D-53105 Bonn, Germany (Reprint); Univ Bonn, Med Ctr, Dept Neuropathol, D-53105 Bonn, Germany; Tartu Univ Clin, Dept Pathol & Neuropathol, Tartu, Estonia. ACTA NEUROPATHOLOGICA (APR 2003) Vol. 105, No. 4, pp. 328-332. ISSN: 0001-6322. Publisher: SPRINGER, 233 SPRING STREET, NEW YORK, NY 10013 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Malignant transformation of human gliomas is accompanied by extensive proliferation of stromal blood vessels. Recent data suggest mesenchymal transdifferentiation of neoplastic cells in various human cancers, including colon and breast cancer as well as gliosarcoma. In this study, we have analyzed proliferating stromal blood vessels in glioblastoma multiforme for the presence of mutations in the tumor suppressor gene TP53. Using tissue arrays derived from glioblastoma specimens, cases with significant immunohistochemical p53 accumulation were selected for molecular genetic detection of TP53 mutations in exons 5 to 8. None of the tumors included in this series displayed properties of gliosarcoma. Proliferating glomeruloid stromal vessels were isolated by laser microdissection from paraffin sections. In six cases, single-strand conformation polymorphism analysis for mutations of the TP53 gene in stromal blood vessels compared with adjacent tumor cells and subsequent DNA sequencing of the resulting DNA fragments were carried out. Glioblastoma cells of these cases exhibited TP53 mutations in exons 5, 7 and 8. None of these tumors showed TP53 mutations in microdissected samples from glomeruloid vessels. The absence of TP53 mutations in vascular stromal components of glioblastoma multiforme supports the hypothesis that microvascular proliferations originate from the tumor stroma and are not derived from transdifferentiated glioblastoma cells.

L7 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2000:154206 Document No.: PREV200000154206. Loss of PTEN facilitates HIF-1-mediated gene expression. Zundel, Wayne; Schindler, Cornelia; Haas-Kogan, Daphne; Koong, Albert; Kaper, Fiona; Chen, Eunice; Gottschalk,

Alexander R.; Ryan, Heather E.; Johnson, Randall S.; Jefferson, Anne B.; Stokoe, David; Giaccia, Amato J. [Reprint author]. Mayer Cancer Biology Research Laboratory, Department of Radiation Oncology, Stanford University, Stanford, CA, 94305-5468, USA. Genes and Development, (Feb. 15, 2000) Vol. 14, No. 4, pp. 391-396. print.
CODEN: GEDEEP. ISSN: 0890-9369. Language: English.

AB In glioblastoma-derived cell lines, PTEN does not significantly alter apoptotic sensitivity or cause complete inhibition of DNA synthesis. However, in these cell lines PTEN regulates hypoxia- and IGF-1-induced angiogenic gene expression by regulating Akt activation of HIF-1 activity. Restoration of wild-type PTEN to glioblastoma cell lines lacking functional PTEN ablates hypoxia and IGF-1 induction of HIF-1-regulated genes. In addition, Akt activation leads to HIF-1alpha stabilization, whereas PTEN attenuates hypoxia-mediated HIF-1alpha stabilization. We propose that loss of PTEN during malignant progression contributes to tumor expansion through the deregulation of Akt activity and HIF-1-regulated gene expression.

L7 ANSWER 6 OF 6 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

1994:564125 The Genuine Article (R) Number: PE799. DETECTION AND QUANTIFICATION OF VASCULAR ENDOTHELIAL GROWTH-FACTOR VASCULAR-PERMEABILITY FACTOR IN BRAIN-TUMOR TISSUE AND CYST FLUID - THE KEY TO ANGIOGENESIS. WEINDEL K (Reprint); MORINGLANE J R; MARME D; WEICH H A. GESELL BIOTECHNOL FORSCH MBH, DEPT GENE EXPRESS, D-38124 BRAUNSCHWEIG, GERMANY; UNIV FREIBURG, CTR TUMOR BIOL, INST MOLEC MED, D-79106 FREIBURG, GERMANY; UNIV SAARLAND, DEPT NEUROSURG, STEREOTAXY SECT, W-6650 HOMBURG, GERMANY. NEUROSURGERY (SEP 1994) Vol. 35, No. 3, pp. 439-448. ISSN: 0148-396X. Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB IN PRIMARY MALIGNANT brain tumors increased vascularity and marked edema strongly suggest a possible role of the vascular endothelial growth factor/vascular permeability factor (VEGF/VPF). This was confirmed by earlier in situ hybridization studies, by analysis of the expression of the mitogen in different subsets of glioblastoma cells, and by the fact that the VEGF/VPF receptor flt-1 (fms-like tyrosine kinase) is up-regulated in tumor cells in vivo. To assess and quantify the expression of the VEGF/VPF gene and of the receptor gene, 26 surgical specimens of brain tumor tissue from 24 patients were analyzed. In most malignant gliomas, the expression level of the VEGF/VPF gene is elevated and can be increased up to 20- to 50-fotd in comparison with low-grade tumors. Using polymerase chain reaction-based amplification, it could be shown that the messenger RNAs of three different VEGF/VPF forms are synthesized in tumor tissue samples. Northern blot studies revealed that in some samples a significant expression of the gene coding for placenta growth factor, a growth factor closely related to VEGF/VPF, was observed. In addition, using a radioreceptor assay it was possible to detect high VEGF/VPF-like activity in the cyst fluids of brain tumors, indicating the accumulation of the mitogen and permeability factor in brain tumor cysts. Further investigations revealed that astrocytoma and glioblastoma cells in culture express the VEGF/VPF gene and secrete the VEGF/VPF protein, whereas gene expression of the two known VEGF/VPF receptors, kinase insert domain-containing receptor and flt-1, could not be detected. These data support previous reports, which stated that VEGF/VPF acts as a paracrine growth and permeability factor in brain tumors and may contribute to tumor growth by initiating tumor angiogenesis.

=> s l4 and VEGF receptor
L8 203 L4 AND VEGF RECEPTOR

=> s l8 and glioblastoma multiforme

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L9            0 L8 AND GLIOBLASTOMA MULTIFORME

=> s l8 and glioblastoma
L10           0 L8 AND GLIOBLASTOMA

=> s l8 and glioblastoma
L11           0 L8 AND GLIOBLASTOMA

=> s l8 and flk-1
L12          58 L8 AND FLK-1

=> s l12 and glioblastoma
L13           0 L12 AND GLIOBLASTOMA

=> s l12 and brain tissue
L14           0 L12 AND BRAIN TISSUE

=> s l8 and brain tissue
L15           0 L8 AND BRAIN TISSUE

=> s VEGF-D
L16        1329 VEGF-D

=> s l16 and brain tissue
L17           4 L16 AND BRAIN TISSUE

=> dup remove l17
PROCESSING COMPLETED FOR L17
L18           4 DUP REMOVE L17 (0 DUPLICATES REMOVED)

=> d l18 1-4 cbib abs

L18  ANSWER 1 OF 4  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
2006:121566  Document No.: PREV200600122161. Method for identifying a test
     compound that modulates expression of a Fra-1 gene in a brain cancer cell.
     Debinski, Waldemar [Inventor]; Gibo, Denise M. [Inventor]. Hershey, PA
     USA. Patent Info.: US 06884581 20050426. Official Gazette of the United
     States Patent and Trademark Office Patents, (APR 26 2005)
     CODEN: OGUPE7. ISSN: 0098-1133. Language: English.
AB   Fra-1 serves as a target for diagnosing and treating glioblastoma
     multiforme and related brain cancers.  Cancer in a brain
     tissue sample is detected by analyzing expression of Fra-1 in the
     sample.  Brain cancer is treated by modulating Fra-1 gene expression in
     cells of the cancer, and by inhibiting angiogenesis associated with the
     cancer by interfering with Fra-1 binding to a VEGF-D
     promoter.

L18  ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
2005:1242850  Document No. 143:476225  Over-expression of tumor antigen Fra-1
     in glioblastoma multiforme and inhibition of Fra-1 binding to a
     VEGF-D promoter for treating brain cancer.  Debinski,
     Waldemar; Gibo, Denise M. (The Penn State Research Foundation, USA).  U.S.
     Pat. Appl. Publ. US 2005260649 A1 20051124, 42 pp., Cont.-in-part of U.S.
     6,884,581.  (English).  CODEN: USXXCO.  APPLICATION: US 2005-104137
     20050412.  PRIORITY: US 2001-268089P 20010212; US 2002-75499 20020212.
AB   The invention relates to the discovery that glioblastoma multiforme (GBM)
     strongly expresses Fra-1, an AP-1 transcription factor.  The gene for
     VEGF-D, a vascular endothelial growth factor that plays
     a role in angiogenesis, harbors an optimal AP-1 binding site within its
     promoter region.  When heterodimerized with c-Jun, Fra-1 binds to the AP-1
     site within the VEGF-D gene promoter and activates
     expression of VEGF-D.  Based on this discovery,
     central nervous system (CNS) cancers such as GBM can be diagnosed and
     treated using Fra-1 as a target tumor antigen.  In addition, by disrupting
     the interaction between Fra-1 and the VEGF-D gene
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promoter, tumor angiogenesis can be inhibited. Cancer in a brain tissue sample is detected by analyzing expression of Fra-1 in the sample. Brain cancer is treated by modulating Fra-1 gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with Fra-1 binding to a VEGF-D promoter.

L18 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

2002:637486 Document No. 137:164115 VEGF-D expression in brain cancer in relation to diagnosis and treatment. Debinski, Waldemar; Gibo, Denise M. (The Penn State Research Foundation, USA). PCT Int. Appl. WO 2002064097 A2 20020822, 43 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US5044 20020212. PRIORITY: US 2001-268089P 20010212.

AB VEGF-D serves as a target for diagnosing and treating glioblastoma multiforme and related brain cancers. Cancer in a brain tissue sample is detected by analyzing expression of VEGF-D in the sample. Brain cancer is treated by modulating VEGF-D gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with VEGF-D binding to a VEGF-D receptor.

L18 ANSWER 4 OF 4 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

2002080155 EMBASE VEGF-D is an X-linked/AP-1 regulated putative onco-angiogen in human glioblastoma multiforme. Debinski W.; Slagle-Webb B.; Achen M.G.; Stacker S.A.; Tulchinsky E.; Gillespie G.Y.; Gibo D.M.. Dr. W. Debinski, Section of Neurosurgery/H110, Department of Surgery, PA State Univ. Coll. of Med., 500 University Drive, Hershey, PA 17033-0850, United States. wdebinski@psu.edu. Molecular Medicine Vol. 7, No. 9, pp. 598-608 2001.
Refs: 50.
ISSN: 1076-1551. CODEN: MOMEE2
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20020314. Last Updated on STN: 20020314

AB Background: Glioblastoma multiforme (GBM) is a hypervascularized and locally infiltrating brain tumor of astroglial origin with a very poor prognosis. An X-linked c-fos oncogene-inducible mitogenic, morphogenic, and angiogenic factor, endothelial growth factor-D (VEGF-D), is the newest mammalian member of VEGF family. We analyzed VEGF-D in GBM because of its high angiogenic potential and its linkage to the X chromosome. Materials and Methods: Nonmalignant brain and GBM tissue sections as well as GBM cell lines were analyzed by immunofluorescence for the expression of VEGF-D, factor VIII (endothelial cell marker), glial-fibrillary acidic protein (GFAP) (astrocytic cell lineage cytoplasmic marker), and several Fos family transcription factors, including c-Fos and Fra-1. The proteins were also detected by Western blots. The differences between genotypes of normal brain and GBM cells were examined by cDNA microarrays. Results and Conclusions: GBM expressed ubiquitously VEGF-D, which colocalized with GFAP. Contrary to our expectations, low levels of c-Fos were detected in GBM cells. However, we identified another Fos family member, Fra-1, together with its transcriptional activation partner, c-Jun, as being stably up-regulated in GBM cells. Furthermore, we demonstrated that a fra-1 transgene induced VEGF-D expression in cultured cells and GBM cell stimulation evoked a sustained increase in both Fra-1 and VEGF-D levels. This study reveals that an up-regulation of AP-1 factors may be a hallmark of GBM.

Because VEGF-D activates VEGF receptor 2 and 3, receptors important for tumor angiogenesis, it may represent an X-linked/AP-1-regulated onco-angiogen in human GBM. The VEGF-D system and AP-1 activity appear to be very attractive targets for new molecular diagnostics and rational molecular anti-cancer therapies.

=> s l16 and brain cancer
L19 3 L16 AND BRAIN CANCER

=> dup remove l19
PROCESSING COMPLETED FOR L19
L20 3 DUP REMOVE L19 (0 DUPLICATES REMOVED)

=> d l20 1-3 cbib abs

L20 ANSWER 1 OF 3 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2006:121566 Document No.: PREV200600122161. Method for identifying a test compound that modulates expression of a Fra-1 gene in a brain cancer cell. Debinski, Waldemar [Inventor]; Gibo, Denise M. [Inventor]. Hershey, PA USA. Patent Info.: US 06884581 20050426. Official Gazette of the United States Patent and Trademark Office Patents, (APR 26 2005)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.
AB Fra-1 serves as a target for diagnosing and treating glioblastoma multiforme and related brain cancers. Cancer in a brain tissue sample is detected by analyzing expression of Fra-1 in the sample. Brain cancer is treated by modulating Fra-1 gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with Fra-1 binding to a VEGF-D promoter.

L20 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
2005:1242850 Document No. 143:476225 Over-expression of tumor antigen Fra-1 in glioblastoma multiforme and inhibition of Fra-1 binding to a VEGF-D promoter for treating brain cancer. Debinski, Waldemar; Gibo, Denise M. (The Penn State Research Foundation, USA). U.S. Pat. Appl. Publ. US 2005260649 A1 20051124, 42 pp., Cont.-in-part of U.S. 6,884,581. (English). CODEN: USXXCO. APPLICATION: US 2005-104137 20050412. PRIORITY: US 2001-268089P 20010212; US 2002-75499 20020212.
AB The invention relates to the discovery that glioblastoma multiforme (GBM) strongly expresses Fra-1, an AP-1 transcription factor. The gene for VEGF-D, a vascular endothelial growth factor that plays a role in angiogenesis, harbors an optimal AP-1 binding site within its promoter region. When heterodimerized with c-Jun, Fra-1 binds to the AP-1 site within the VEGF-D gene promoter and activates expression of VEGF-D. Based on this discovery, central nervous system (CNS) cancers such as GBM can be diagnosed and treated using Fra-1 as a target tumor antigen. In addition, by disrupting the interaction between Fra-1 and the VEGF-D gene promoter, tumor angiogenesis can be inhibited. Cancer in a brain tissue sample is detected by analyzing expression of Fra-1 in the sample. Brain cancer is treated by modulating Fra-1 gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with Fra-1 binding to a VEGF-D promoter.

L20 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
2002:637486 Document No. 137:164115 VEGF-D expression in brain cancer in relation to diagnosis and treatment. Debinski, Waldemar; Gibo, Denise M. (The Penn State Research Foundation, USA). PCT Int. Appl. WO 2002064097 A2 20020822, 43 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US5044 20020212. PRIORITY: US 2001-268089P 20010212.

AB VEGF-D serves as a target for diagnosing and treating glioblastoma multiforme and related brain cancers. Cancer in a brain tissue sample is detected by analyzing expression of VEGF-D in the sample. Brain cancer is treated by modulating VEGF-D gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with VEGF-D binding to a VEGF-D receptor.

=> s l16 and x chromosome
L21 13 L16 AND X CHROMOSOME

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PROCESSING COMPLETED FOR L21
L22 6 DUP REMOVE L21 (7 DUPLICATES REMOVED)

=> d l22 1-6 cbib abs

L22 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
2006:522297 Document No. 145:181711 Histone modification patterns associated with the human X chromosome. Brinkman, Arie B.; Roelofsen, Thijs; Pennings, Sebastiaan W. C.; Martens, Joost H. A.; Jenuwein, Thomas; Stunnenberg, Hendrik G. (Department of Molecular Biology, Nijmegen Centre for Molecular Life Sciences, NCMLS M850/3.79, Radboud University, Nijmegen, 6500 HB, Neth.). EMBO Reports, 7(6), 628-634 (English) 2006. CODEN: ERMEAX. ISSN: 1469-221X. Publisher: Nature Publishing Group.

AB X inactivation is associated with chromosome-wide establishment of inactive chromatin. Although this is classically regarded as facultative heterochromatin that is uniform in nature, the exact distribution of associated epigenetic marks is not well defined. Here the authors have analyzed histone modifications in human somatic cells within two selected regions of the X chromosome. Intergenic, coding and promoter regions are segregated into differentially marked chromatin. H3K27me3 is most prominent in intergenic and silenced coding regions, but is associated with some active coding regions as well. Histone H3/H4 acetylation and H3K4me3 are locally enriched at promoter regions but do not necessarily mark continuing transcription. Remarkably, H3K9me3 is predominant in coding regions of active genes, a phenomenon that is not restricted to the X chromosome. These results argue against the exclusiveness of individual marks to heterochromatin or euchromatin, but rather suggest that composite patterns of interdependent or mutually exclusive modifications together signal the gene expression status.

L22 ANSWER 2 OF 6 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
2006:21564 The Genuine Article (R) Number: 995MA. Genetic background of HSH in three Polish families and a patient with an X;9 translocation. Jalkanen R (Reprint); Pronicka E; Tyynismaa H; Hanauer A; Walder R; Alitalo T. Univ Helsinki, Dept Obstet & Gynecol, Biomedicum Helsinki, Cent Hosp, Haartmaninkatu 8, POB 700, Helsinki 00029, Finland (Reprint); Univ Helsinki, Dept Obstet & Gynecol, Biomedicum Helsinki, Cent Hosp, Helsinki 00029, Finland; Univ Helsinki, Dept Med Genet, Helsinki 00029, Finland; Childrens Mem Hlth Inst, Dept Paediat, Div Metab Dis, Warsaw, Poland; CNRS, INSERM, Inst Genet & Biol Mol & Cellulaire, Strasbourg, France; Univ

Iowa, Dept Pediat, Iowa City, IA 52242 USA; Univ Iowa, Howard Hughes Med Inst, Iowa City, IA 52242 USA. reetta.jalkanen@helsinki.fi. EUROPEAN JOURNAL OF HUMAN GENETICS (JAN 2006) Vol. 14, No. 1, pp. 55-62. ISSN: 1018-4813. Publisher: NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Hypomagnesemia with secondary hypocalcemia (HSH) is a rare inherited disease, characterised by neurological symptoms, such as tetany, muscle spasms and seizures, due to hypocalcemia. It has been suggested that HSH is genetically heterogeneous, but only one causative gene, TRPM6, on chromosome 9 has so far been isolated. We have now studied the genetic background of HSH in four Polish patients belonging to three families, and a HSH patient carrying an apparently balanced X; 9 translocation. The translocation patient has long been considered as an example of the X-linked form of HSH. We identified six TRPM6 gene mutations, of which five were novel, in the Polish patients. All the alterations were either nonsense/splicing or missense mutations. The clinical picture of the patients was similar to the HSH patients reported earlier. No genotype-phenotype correlation could be detected. Sequencing did not reveal any TRPM6 or TRPM7 gene mutations in the female HSH patient with an X; 9 translocation. Isolation of the translocation breakpoint showed that the chromosome 9 specific breakpoint mapped within satellite III repeat sequence. The X-chromosomal breakpoint was localised to the first intron of the vascular endothelial growth factor gene, VEGFD. No other sequence alterations were observed within the VEGFD gene. Even though the VEGFD gene was interrupted by the X; 9 translocation, it seems unlikely that VEGFD is causing the translocation patient's HSH-like phenotype. Furthermore, re-evaluation of patient's clinical symptoms suggests that she did not have a typical HSH.

L22 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2003:492648 Document No.: PREV200300487100. Epigenetics in high-grade astrocytomas: Opportunities for prevention and detection of brain tumors. Debinski, Waldemar [Reprint Author]; Gibo, Denise; Mintz, Akiva. Section of Neurosurgery, Department of Surgery, College of Medicine, Pennsylvania State University, 500 University Drive, H110, Hershey, PA, 17033-0850, USA. wdebinski@psu.edu. Verma, Mukesh [Editor, Reprint Author]; Dunn, Barbara K. [Editor, Reprint Author]; Umar, Asad [Editor, Reprint Author]. (2003) pp. 232-242. Epigenetics in cancer prevention: Early detection and risk assessment. print. Publisher: New York Academy of Sciences, 2 East 63rd Street, New York, NY, 10021, USA. Series: Annals of the New York Academy of Sciences.
Meeting Info.: Workshop on Epigenetics in Cancer Prevention: Early Detection and Risk Assessment. Bethesda, MD, USA. December 03-04, 2001. National Institutes of Health (NIH).
ISSN: 0077-8923 (ISSN print). ISBN: 1-57331-430-7 (cloth). Language: English.

L22 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 1
2003204925. PubMed ID: 12724228. Epigenetics in high-grade astrocytomas: opportunities for prevention and detection of brain tumors. Debinski Waldemar; Gibo Denise; Mintz Akiva. (Department of Neurosurgery, Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033-0850, USA.. wdebinski@psu.edu) . Annals of the New York Academy of Sciences, (2003 Mar) Vol. 983, pp. 232-42. Ref: 60. Journal code: 7506858. ISSN: 0077-8923. Pub. country: United States. Language: English.

AB Human high-grade astrocytomas (HGA) are the most prevalent incurable brain tumors. We found that the vast majority of HGA patients overexpress a restricted receptor for an immune regulatory cytokine, interleukin 13 (IL-13). Interestingly, the HGA-associated restricted receptor protein IL-13Ralpha2 is expressed in the testes, and its gene is localized to chromosome X. These mirror the expression pattern and genomic localization of cancer/testes tumor antigens (CTA). Hypothetical considerations and now experimental evidence are beginning to point towards epigenetics, and DNA methylation alterations in particular, as

being responsible for the appearance in cancer of CTA, including IL-13Ralpha2. In line with our interest in the X chromosome and oncogenesis, we have identified a new ubiquitous angiogenic factor in HGA, a vascular endothelial growth factor-D (VEGF-D). We have also demonstrated that the activating protein-1 (AP-1) family of transcription factors play a potentially critical role in the progression of gliomas by eliciting uncontrolled upregulation of VEGF-D and other compounds essential for cancer cell proliferation, tumorigenesis, and infiltration. The possibility exists that an unopposed constitutive increase in AP-1 activity in HGA is related to epigenetic silencing of the inhibitors of AP-1 activity. These phenomena offer potential targets for exploitation in either prevention or early detection of brain tumors. For example, anticancer vaccines against shared CTA could help in prevention of HGA development. Furthermore, drugs with anti-AP-1 activity could be effective in preventing formation/progression of HGA, or progression from less malignant lower grade gliomas to HGA. Also, circulating antibodies against CTA and factors that are AP-1 regulated may provide a useful tool in early detection of brain tumors or for monitoring their progression following initial treatment.

L22 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 2

2002052394. PubMed ID: 11778649. VEGF-D is an X-linked/AP-1 regulated putative onco-angiogen in human glioblastoma multiforme. Debinski W; Slagle-Webb B; Achen M G; Stacker S A; Tulchinsky E; Gillespie G Y; Gibo D M. (Division of Neurosurgery, Pennsylvania State University College of Medicine, Hershey 17033-0850, USA.. wdebinski@psu.edu) . Molecular medicine (Cambridge, Mass.), (2001 Sep) Vol. 7, No. 9, pp. 598-608. Journal code: 9501023. ISSN: 1076-1551. Pub. country: United States. Language: English.

AB BACKGROUND: Glioblastoma multiforme (GBM) is a hypervascularized and locally infiltrating brain tumor of astroglial origin with a very poor prognosis. An X-linked c-fos oncogene-inducible mitogenic, morphogenic, and angiogenic factor, endothelial growth factor-D (VEGF-D), is the newest mammalian member of VEGF family. We analyzed VEGF-D in GBM because of its high angiogenic potential and its linkage to the X chromosome. MATERIALS AND METHODS: Nonmalignant brain and GBM tissue sections as well as GBM cell lines were analyzed by immunofluorescence for the expression of VEGF-D, factor VIII (endothelial cell marker), glial-fibrillary acidic protein (GFAP) (astrocytic cell lineage cytoplasmic marker), and several Fos family transcription factors, including c-Fos and Fra-1. The proteins were also detected by Western blots. The differences between genotypes of normal brain and GBM cells were examined by cDNA microarrays. RESULTS AND CONCLUSIONS: GBM expressed ubiquitously VEGF-D, which colocalized with GFAP. Contrary to our expectations, low levels of c-Fos were detected in GBM cells. However, we identified another Fos family member, Fra-1, together with its transcriptional activation partner, c-Jun, as being stably up-regulated in GBM cells. Furthermore, we demonstrated that a fra-1 transgene induced VEGF-D expression in cultured cells and GBM cell stimulation evoked a sustained increase in both Fra-1 and VEGF-D levels. This study reveals that an up-regulation of AP-1 factors may be a hallmark of GBM. Because VEGF-D activates VEGF receptor 2 and 3, receptors important for tumor angiogenesis, it may represent an X-linked/AP-1-regulated onco-angiogen in human GBM. The VEGF-D system and AP-1 activity appear to be very attractive targets for new molecular diagnostics and rational molecular anti-cancer therapies.

L22 ANSWER 6 OF 6 MEDLINE on STN

97349118. PubMed ID: 9205122. Molecular cloning of a novel vascular endothelial growth factor, VEGF-D. Yamada Y; Nezu J; Shimane M; Hirata Y. (Gene Search Program, Chugai Research Institute for Molecular Medicine, Niihari, Ibaraki, Japan.. yamaday@tk.chugai-

pharm.co.jp) . Genomics, (1997 Jun 15) Vol. 42, No. 3, pp. 483-8. Journal code: 8800135. ISSN: 0888-7543. Pub. country: United States. Language: English.

AB We have identified and characterized a novel vascular endothelial growth factor (VEGF), VEGF-D, which is structurally related to vascular endothelial growth factor C. A full-length cDNA for human VEGF-D was cloned following the identification of an EST obtained through a TFASTA search of public EST databases. The murine VEGF-D was subsequently isolated from a mouse lung cDNA library. The human VEGF-D gene was mapped to human chromosome Xp22.31. Both human and mouse VEGF-D are strongly expressed in lung and encode the eight cysteine residues that are highly conserved among the members of this family. The high level of conservation between mouse and human VEGF-D may emphasize the biological importance of this gene. Recently the murine gene, FIGF, which is identical to mouse VEGF-D, was reported.

=> s glioblastoma multiforme
L23 14897 GLIOBLASTOMA MULTIFORME

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L24 12 L23 AND CHROMOSOME X

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L25 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2006:75914 Document No.: PREV200600069745. Overexpressed Skp2 within 5p amplification detected by array-based comparative genomic hybridization is associated with poor prognosis of glioblastomas. Saigusa, Kuniyasu; Hashimoto, Naoya; Tsuda, Hitoshi; Yokoi, Sana; Maruno, Motohiko; Yoshimine, Toshiki; Aoyagi, Masaru; Ohno, Kikuo; Imoto, Issei; Inazawa, Johji [Reprint Author]. Tokyo Med and Dent Univ, Med Res Inst, Dept Mol Cytogenet, Bunkyo Ku, 1-5-45 Yushima, Tokyo 1138510, Japan. johinaz.cgen@mri.tmd.ac.jp. Cancer Science, (OCT 2005) Vol. 96, No. 10, pp. 676-683.
ISSN: 1347-9032. Language: English.

AB To better understand the pathogenesis of glioblastoma multiforme (GBM) and to increase the accuracy of predicting outcomes for patients with this disease, we performed genome-wide screening for DNA copy-number aberrations in 22 glioma-derived cell lines using a custom-made comparative genomic hybridizationarray. Copy-number gains were frequently detected at 3q, 7p, 7q, 20q, Xp and Xq, and losses at 4q, 9p, 10p, 10q, 11q, 13q, 14q, 18q, and 22q. Among several non-random chromosomal aberrations, the gain/amplification of DNA at 5p, which has never been reported before in GBM, was detected with a relatively high ratio (log2 ratio = 0.41-1.19) in four cell lines. Amplification and subsequent overexpression of SKP2, a possible target of amplification within 5p, were detected in four of the 22 cell lines. We also investigated the expression of the gene product in primary GBM by immunohistochemistry, which revealed increased levels of Skp2 in 11 of the 35 tumors examined (31.4%). Heightened expression of Skp2 was associated with shorter overall survival (P = 0.001, logrank test), especially in patients younger than 65 years. These results suggest that overexpression of Skp2 through gene amplification may contribute to the pathogenesis of GBM, and that overabundance of the protein might be a useful prognostic tool in patients with this disease.

L25 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
2003:270223 Document No. 138:266964 Gene expression profiles useful in

methods of diagnosis of cancer compositions and methods of screening for modulators of cancer. Afar, Daniel; Aziz, Natasha; Gish, Kurt C.; Hevezi, Peter A.; Mack, David H.; Wilson, Keith E.; Zlotnik, Albert (EOS Biotechnology, Inc., USA). PCT Int. Appl. WO 2003025138 A2 20030327, 767 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-XD29560 20020917. PRIORITY: US 2001-323469P 20010917; US 2001-323887P 20010920; US 2001-350666P 20011113; US 2002-355145P 20020208; US 2002-355257P 20020208; US 2002-372246P 20020412; WO 2002-US29560 20020917.

AB Described herein are genes whose expression are up-regulated or down-regulated in specific cancers, including acute lymphocytic leukemia, glioblastoma, glioblastoma multiforme, glioma, kidney cancer, stomach cancer, melanoma, and benign NEVI. Mol. profiles of various normal and cancerous tissues were determined and analyzed using the Affymetrix/Eos Hu01 and Hu03 GeneChip microarrays containing 35,403 and 59,680 probe sets, resp. Related methods and compns. that can be used for diagnosis and treatment of those cancers are disclosed. Also described herein are methods that can be used to identify modulators of selected cancers. [This abstract record is one of nine records for this documents necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L25 ANSWER 3 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2000:216414 Document No.: PREV200000216414. Spectral karyotyping (SKY) of human brain tumors. Li, X.-N. [Reprint author]; Harris, C. P. [Reprint author]; Lu, X. Y. [Reprint author]; Perlaky, L. [Reprint author]; Lau, C. C. [Reprint author]. Texas Children's Hospital, Baylor Coll of Medicine, Houston, TX, USA. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2000) No. 41, pp. 418-419. print. Meeting Info.: 91st Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 01-05, 2000. ISSN: 0197-016X. Language: English.

L25 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 2
1999168408. PubMed ID: 10070860. Genetic aberrations in glioblastoma multiforme: translocation of chromosome 10 in an O-2A-like cell line. Mao X; Jones T A; Tomlinson I; Rowan A J; Fedorova L I; Zelenin A V; Mao J I; Gutowski N J; Noble M; Sheer D. (Human Cytogenetics Laboratory, Imperial Cancer Research Fund, London, UK.) British journal of cancer, (1999 Feb) Vol. 79, No. 5-6, pp. 724-31. Journal code: 0370635. ISSN: 0007-0920. Pub. country: SCOTLAND: United Kingdom. Language: English.

AB We have examined the genetic aberrations in two near-diploid glioblastoma multiforme cell lines that appear to have arisen from different glial lineages. One cell line, Hu-O-2A/Gb1, expresses antigens and metabolic profiles characteristic of the oligodendrocyte-type-2 astrocyte (O-2A) lineage of the rat central nervous system. This line generates, in vitro, cells with characteristics of O-2A progenitor cells, oligodendrocytes and astrocytes. The second cell line, IN1434, is derived from an astrocyte or a precursor cell restricted to astrocytic differentiation. In Hu-O-2A/Gb1 the sole homologue of chromosome 10 is disrupted at band 10p11-12.1 by translocation with chromosomes X and 15. The translocation breakpoint is localized between genetic markers D10S2103 and [D10S637, D10S1962, D10S355]. Other aberrations include a 5;14 translocation, deletion of the long and short arms of chromosome 16 and loss of one copy of the CDKN2 gene. IN1434 cells share some cytogenetic abnormalities with Hu-O-2A/Gb1 cells, despite their apparent derivation from a different biological

origin, but also have translocations involving the long and short arms of chromosome 1 and the long arm of chromosome 7, and deletion of chromosome 13 at bands 13q12-21.

L25 ANSWER 5 OF 5 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
1997:182246 The Genuine Article (R) Number: WK746. Analysis of sex chromosomal numerical aberrations in human astrocytomas by FISH. Liu X Q (Reprint); Numa Y; Kasai H; Tsuchida T; Kawamoto K. KANSAI MED UNIV, DEPT NEUROSURG, MORIGUCHI, OSAKA 570, JAPAN. INTERNATIONAL JOURNAL OF ONCOLOGY (MAR 1997) Vol. 10, No. 3, pp. 497-502. ISSN: 1019-6439. Publisher: INT JOURNAL ONCOLOGY, C/O PROFESSOR D A SPANDIDOS, EDITORIAL OFFICE, 1, S MERKOURI ST, ATHENS 116 35, GREECE. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Although sex chromosomal aberrations in astrocytomas have been frequently reported by cytogeneticists, their biologic significance is still unclear. The aim of this study was to investigate sex chromosomal aberrations of astrocytomas by fluorescence in situ hybridization (FISH) and to determine whether there is a relationship between these aberrations and abnormalities of chromosomes 7 and 10. The astrocytoma specimens were obtained from 14 male and 11 female patients. The centromeric probes DYZ1, DXZ1, D7Z1 and D10Z1 were used to determine the numerical changes in chromosomes Y, X, 7, and 10 by FISH. The hybridization spots were counted by fluorescence microscopy. Three cases showed chromosome X aberrations, including two cases with loss of chromosome X and one case with a complex chromosome X aberration among 11 female astrocytomas. Eight cases with loss of chromosome Y were seen among 14 male astrocytomas; one was grade II, three grade III, and four grade IV tumors. One case of disomy X was observed among male grade II tumors. Seven of the eight tumors with loss of chromosome Y had additional complex chromosome aberrations. Our results suggest that sex chromosome aberrations in malignant astrocytomas are non-random and frequent. These changes suggest an association with aberrations of chromosomes 7 and 10. These sex chromosome aberrations seem to be a part of a complex chromosome pattern of aberrations in astrocytomas. The observed abnormalities may not necessarily be a part of the neoplastic progression in malignant astrocytomas, but they may be of biologic significance.

=> s (debinski w?/au or gibo d?/au)
L26 615 (DEBINSKI W?/AU OR GIBO D?/AU)

=> s l26 and glioblastoma multiforme
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L29 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2006:121566 Document No.: PREV200600122161. Method for identifying a test compound that modulates expression of a Fra-1 gene in a brain cancer cell. Debinski, Waldemar [Inventor]; Gibo, Denise M. [Inventor]. Hershey, PA USA. Patent Info.: US 06884581 20050426. Official

Gazette of the United States Patent and Trademark Office Patents, (APR 26 2005)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB Fra-1 serves as a target for diagnosing and treating glioblastoma multiforme and related brain cancers. Cancer in a brain tissue sample is detected by analyzing expression of Fra-1 in the sample. Brain cancer is treated by modulating Fra-1 gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with Fra-1 binding to a VEGF-D promoter.

L29 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

2005:1242850 Document No. 143:476225 Over-expression of tumor antigen Fra-1 in glioblastoma multiforme and inhibition of Fra-1 binding to a VEGF-D promoter for treating brain cancer. Debinski, Waldemar; Gibo, Denise M. (The Penn State Research Foundation, USA). U.S. Pat. Appl. Publ. US 2005260649 A1 20051124, 42 pp., Cont.-in-part of U.S. 6,884,581. (English). CODEN: USXXCO. APPLICATION: US 2005-104137 20050412. PRIORITY: US 2001-268089P 20010212; US 2002-75499 20020212.

AB The invention relates to the discovery that glioblastoma multiforme (GBM) strongly expresses Fra-1, an AP-1 transcription factor. The gene for VEGF-D, a vascular endothelial growth factor that plays a role in angiogenesis, harbors an optimal AP-1 binding site within its promoter region. When heterodimerized with c-Jun, Fra-1 binds to the AP-1 site within the VEGF-D gene promoter and activates expression of VEGF-D. Based on this discovery, central nervous system (CNS) cancers such as GBM can be diagnosed and treated using Fra-1 as a target tumor antigen. In addition, by disrupting the interaction between Fra-1 and the VEGF-D gene promoter, tumor angiogenesis can be inhibited. Cancer in a brain tissue sample is detected by analyzing expression of Fra-1 in the sample. Brain cancer is treated by modulating Fra-1 gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with Fra-1 binding to a VEGF-D promoter.

L29 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

2002:637486 Document No. 137:164115 VEGF-D expression in brain cancer in relation to diagnosis and treatment. Debinski, Waldemar; Gibo, Denise M. (The Penn State Research Foundation, USA). PCT Int. Appl. WO 2002064097 A2 20020822, 43 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US5044 20020212. PRIORITY: US 2001-268089P 20010212.

AB VEGF-D serves as a target for diagnosing and treating glioblastoma multiforme and related brain cancers. Cancer in a brain tissue sample is detected by analyzing expression of VEGF-D in the sample. Brain cancer is treated by modulating VEGF-D gene expression in cells of the cancer, and by inhibiting angiogenesis associated with the cancer by interfering with VEGF-D binding to a VEGF-D receptor.

L29 ANSWER 4 OF 5 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

2002080155 EMBASE VEGF-D is an X-linked/AP-1 regulated putative onco-angiogen in human glioblastoma multiforme. Debinski W. ; Slagle-Webb B.; Achen M.G.; Stacker S.A.; Tulchinsky E.; Gillespie G.Y.; Gibo D.M.. Dr. W. Debinski, Section of Neurosurgery/H110, Department of Surgery, PA State Univ. Coll. of Med., 500 University Drive, Hershey, PA 17033-0850, United States. wdebinski@psu.edu. Molecular Medicine Vol. 7, No. 9, pp. 598-608 2001.
Refs: 50.
ISSN: 1076-1551. CODEN: MOMEE2

Pub. Country: United States. Language: English. Summary Language: English. Entered STN: 20020314. Last Updated on STN: 20020314

AB Background: Glioblastoma multiforme (GBM) is a hypervascularized and locally infiltrating brain tumor of astroglial origin with a very poor prognosis. An X-linked c-fos oncogene-inducible mitogenic, morphogenic, and angiogenic factor, endothelial growth factor-D (VEGF-D), is the newest mammalian member of VEGF family. We analyzed VEGF-D in GBM because of its high angiogenic potential and its linkage to the X chromosome. Materials and Methods: Nonmalignant brain and GBM tissue sections as well as GBM cell lines were analyzed by immunofluorescence for the expression of VEGF-D, factor VIII (endothelial cell marker), glial-fibrillary acidic protein (GFAP) (astrocytic cell lineage cytoplasmic marker), and several Fos family transcription factors, including c-Fos and Fra-1. The proteins were also detected by Western blots. The differences between genotypes of normal brain and GBM cells were examined by cDNA microarrays. Results and Conclusions: GBM expressed ubiquitously VEGF-D, which colocalized with GFAP. Contrary to our expectations, low levels of c-Fos were detected in GBM cells. However, we identified another Fos family member, Fra-1, together with its transcriptional activation partner, c-Jun, as being stably up-regulated in GBM cells. Furthermore, we demonstrated that a fra-1 transgene induced VEGF-D expression in cultured cells and GBM cell stimulation evoked a sustained increase in both Fra-1 and VEGF-D levels. This study reveals that an up-regulation of AP-1 factors may be a hallmark of GBM. Because VEGF-D activates VEGF receptor 2 and 3, receptors important for tumor angiogenesis, it may represent an X-linked/AP-1-regulated onco-angiogen in human GBM. The VEGF-D system and AP-1 activity appear to be very attractive targets for new molecular diagnostics and rational molecular anti-cancer therapies.

L29 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 1

1999357905. PubMed ID: 10427128. Receptor for interleukin 13 is abundantly and specifically over-expressed in patients with glioblastoma multiforme. Debinski W; Gibo D M; Slagle B; Powers S K; Gillespie G Y. (Section of Neuro-surgery/H110, Department of Surgery, Pennsylvania State University College of Medicine, Hershey, PA 17033-0850, USA.) International journal of oncology, (1999 Sep) Vol. 15, No. 3, pp. 481-6. Journal code: 9306042. ISSN: 1019-6439. Pub. country: Greece. Language: English.

AB We have recently documented that the vast majority of patients with glioblastoma multiforme (GBM) over-express a receptor (R) for interleukin 13 (IL13) in situ. We have now evaluated further the degree of relative specificity of the binding of IL13 to GBM when compared with other growth factor receptors. Tumor samples of 11 patients with GBM, 7 various normal brain samples, and several cell lines in culture were examined. Same patient tissue sections were incubated with 125I-labeled: IL13, monoclonal antibody HB21 against human transferrin (Tf) receptor, epidermal growth factor (EGF), and an IL4 antagonist, IL4.Y124D. All 11 GBMs stained specifically, densely, and relatively homogeneously for both IL13R and TfR. Seven GBM specimens showed specific binding for 125I-EGF, but it was less homogeneous when compared with IL13R or TfR. Two of the GBMs studied demonstrated extremely high density of the EGFR. Furthermore, we did not detect significant presence of the IL4R in the studied GBM specimens in situ. All sections of non-malignant brain tissues examined showed avid binding by the TfR with lack of consistent and specific binding of 125I-IL13 or -EGF. Thus, it appears that the GBM-associated IL13R is considerably more specific to GBM that the one for Tf and more frequently and homogeneously expressed than the EGFR. These results render further support for the hIL13R being a new unique candidate for delivery of variety of anti-GBM therapies.

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L31 ANSWER 1 OF 4 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 1
2005498297 EMBASE EphA2 as a novel molecular marker and target in glioblastoma multiforme. Wykosky J.; Gibo D.M. ; Stanton C.; Debinski W.. W. Debinski, Comprehensive Cancer Center, Department of Neurosurgery, Wake Forest University School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, United States. debinski@wfubmc.edu. Molecular Cancer Research Vol. 3, No. 10, pp. 541-551 2005.
Refs: 44.
ISSN: 1541-7786. CODEN: MCROC5
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20051208. Last Updated on STN: 20051208
AB We investigated the presence of EphA2, and its ligand, ephrinA1, in glioblastoma multiforme (GBM), a malignant neoplasm of glial cells, and normal brain. We also initially examined the functional importance of the interaction between EphA2 and ephrinA1 in glioma cells. Expression and localization of EphA2 and ephrinA1 in human GBM and normal brain were examined using Western blotting, immunofluorescence, and immunohistochemistry. A functional role for EphA2 was investigated by assessing the activation status of the receptor and the effect of ephrinA1 on the anchorage-independent growth and invasiveness of GBM cells. We found EphA2 to be elevated in .apprx.90% of GBM specimens and cell lines but not in normal brain, whereas ephrinA1 was present at consistently low levels in both GBM and normal brain. EphA2 was activated and phosphorylated by ephrinA1 in GBM cells. Furthermore, ephrinA1 induced a prominent, dose-dependent inhibitory effect on the anchorage-independent growth and invasiveness of GBM cells highly overexpressing EphA2, which was not seen in cells expressing low levels of the receptor. Thus, EphA2 is both specifically overexpressed in GBM and expressed differentially with respect to its ligand, ephrinA1, which may reflect on the oncogenic processes of malignant glioma cells. EphA2 seems to be functionally important in GBM cells and thus may play an important role in GBM pathogenesis. Hence, EphA2 represents a new marker and novel target for the development of molecular therapeutics against GBM. Copyright .COPYRGT. 2005 American Association for Cancer Research.

L31 ANSWER 2 OF 4 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
2005176459 EMBASE Fos-related antigen 1 modulates malignant features of glioma cells. Debinski W.; Gibo D.M.. W. Debinski, Brain Tumor Center of Excellence, Department of Neurosurgery, Wake Forest Univ. School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, United States. debinski@wfubmc.edu. Molecular Cancer Research Vol. 3, No. 4, pp. 237-249 2005.
Refs: 49.
ISSN: 1541-7786. CODEN: MCROC5
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20050505. Last Updated on STN: 20050505
AB Malignant gliomas, and high-grade gliomas (HGG) in particular, are nonmetastasizing but locally infiltrating, hypervascularized brain tumors of poor prognosis. We found previously that a c-fos-inducible vascular endothelial growth factor D is ubiquitously up-regulated in HGG grade IV, glioblastoma multiforme, and that glioblastoma multiforme overexpress Fos-related antigen 1 (Fra-1) rather than the c-Fos. We have thus become interested in the role Fra-1 may play in malignant glioma progression/maintenance, because Fra-1 has the capacity to modulate transcription of a variety of target genes. In this work, we have analyzed the biological effects of ectopic Fra-1 expression or Fra-1

knockdown in malignant glioma cells. Ectopic Fra-1 induced prominent phenotypic changes in all three malignant glioma cell lines examined: H4, U-87 MG, and A-172 MG. These changes were reflected in cells becoming more elongated with larger number of cellular processes. Furthermore, Fra-1 transgene caused H4 cells, which do not form tumor xenografts, to regain tumorigenic capacity. The genotype of these cells changed too, because 50 of 1,056 genes examined became either up- or down-regulated. Conversely, Fra-1 knockdown altered prominently the morphology, anchorage-independent growth, tumorigenic potential, and Fra-1 effector expression, such as vascular endothelial growth factor D, in HGG cells. For example, cells transfected with antisense fra-1 showed shorter cellular processes than the control cells that did not grow in agar, and their tumorigenic potential was significantly diminished. Thus, Fra-1 may likely play an important role in the maintenance/progression of malignant gliomas and potentially represents a new target for therapeutic interventions. Copyright .COPYRGT. 2005 American Association for Cancer Research.

L31 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
1998:163693 Document No. 128:201051 Interleukin fusion proteins and antagonists for targeting of antitumor agents to interleukin 13 receptor-presenting tumors. Debinski, Waldemar; Puri, Raj K. (Penn State Research Foundation, USA). PCT Int. Appl. WO 9808957 A1 19980305, 111 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US15050 19970827. PRIORITY: US 1996-706207 19960830.
AB A method of targeting cytotoxins to tumor cells presenting the interleukin 13 receptor is described. The cytotoxin is administered as a fusion protein with interleukin 13 receptor ligand, e.g. interleukin 13 or anti-receptor antibodies, in combination with an interleukin 4 antagonist to minimize the binding of interleukin 13 to the interleukin 4 receptor that it shares subunits with. A fusion protein of interleukin 13 and Pseudomonas exotoxin was manufactured by expression of the gene in Escherichia coli. The protein was cytotoxic to a number of tumor cell lines. The cytotoxicity was antagonized by interleukin 13 and interleukin 4, but not interleukin 2. Interleukins 13 and 4 bind to common sites on tumor cells but have different effects on the cells. Interleukin 13 activity did not require the p140 subunit of the interleukin 4 receptor and this subunit confers interleukin 4 specificity.

L31 ANSWER 4 OF 4 MEDLINE on STN DUPLICATE 2
1999215813. PubMed ID: 10201630. An immune regulatory cytokine receptor and glioblastoma multiforme: an unexpected link.
Debinski W. (Department of Surgery, Pennsylvania State University College of Medicine, Hershey 17033-0850, USA.) Critical reviews in oncogenesis, (1998) Vol. 9, No. 3-4, pp. 255-68. Ref: 81. Journal code: 8914610. ISSN: 0893-9675. Pub. country: United States. Language: English.
AB Human high-grade gliomas (HGG) are one of the most devastating human malignancies. They are rapidly progressing heterogenous tumors for which no curable treatment is available. Although these tumors are believed to be of glial cell origin, known tumor-specific markers do not characterize them. The specific environmental conditions that cause or promote the development of HGG are not known. The pathomechanism of HGG is yet to be revealed, although more specific genetic alterations are assigned to HGG. Recently, we have found that HGG overexpress a receptor for an immune regulatory cytokine, interleukin-13 (IL-13). In fact, it appears that all patients with glioblastoma multiforme may possess this receptor. IL-13 is an antiinflammatory cytokine with many overlapping functions to its homologue, IL-4. There is a high degree of specificity of the overexpression of the IL-13 receptor in HGG. This

receptor is not only quantitatively but also qualitatively different from the only known functional signaling receptor for IL-13 of normal tissue. It is not shared with IL-4. The more restrictive receptor for IL-13 thus may represent a new factor specific for a disease as heterogenous as HGG.

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---Logging off of STN---

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